Remarks

Claims 1, 3-5, 11-13, 22, 23, 25, and 38-43 are currently pending. Claims 1, 3, 4, 12, 13, 22, 25, and 38-40 stand rejected under 102(b). Applicants respectfully traverse the rejections.

Rejections Under 35 U.S.C. §102(b)

Claims 1, 3, 4, 12, 13, 25, and 40 stand rejected under 35 U.S.C. §102(b) as being anticipated by Keifer (U.S. Pat. No. 5,620,867). The Examiner contends that Keifer discloses a BMP that contains the same sequence as BBP and thus anticipates the claimed SEQ ID No: 1 and inherently anticipates the claimed effects of BBP. The Examiner also argues that the claims do not require that "the claimed peptide increase the degree or rate of osteogenesis or calcification." However claims 1, 3-4, 12, 13, 25, and 40 require that the claimed peptide increase the degree or rate of osteogenesis or calcification.

Applicants respectfully disagree with the Examiner's view of Keifer's teachings. For a prior art reference to anticipate the claimed invention, the prior art reference must contain every element of the claimed invention. *See Zenith Electronics v. PDI Communications Systems*, 522 F.3d 1348, 1363 (Fed. Cir. 2008). As explained in the Declaration of Keyvan Behnam, Ph.D., enclosed with this Request for Continued Examination, the protein that Keifer disclosed in Figures 3 and 5 is secreted phosphoprotein-24 (Spp-24). In contrast, the rejected claims are drawn to substantially pure BBP, a 2.1 kD peptide derived from the 24 kD phosphoprotein Spp-24. *See, e.g.,* Specification, ¶26. The claimed BBP and Spp-24 are not the same molecule. In fact, BBP is approximately 1/12th the size of the Spp-24 protein described in Keifer. Thus, Keifer does not disclose BBP, much less substantially pure BBP.

Further, the claimed BBP peptide increases the rate or degree of osteogenesis or calcification, including in combination with BMP-2 and other BMPs. In contrast, there is no express or inherent evidence that Spp-24 increases the rate or degree of osteogenesis or calcification. Rather, to the contrary, studies have shown that the full length Spp-24 molecule, when combined with BMP, completely inhibits bone formation. *See* Declaration of Keyvan Behnam, at ¶ 9. Thus, Keifer cannot anticipate the claimed invention because Keifer does not disclose the BBP, a 2.1 kD peptide that increases the rate or degree of osteogenesis or calcification.

The Examiner then argues that because the full-length Spp-24 protein disclosed in Keifer contains the BBP peptide, Keifer's disclosure inherently anticipates the claimed invention. The Examiner contends that "insofar as Keifer discloses a peptide comprising the amino acid sequence of SEQ ID NO: 1, then Keifer discloses....a peptide comprising any fragment of SEQ ID NO: 1, wherein the fragment increases the degree or rate of osteogenesis or calcification." However, "[u]nder the doctrine of inherency, if an element is not expressly disclosed in a prior art reference, the reference will still be deemed to anticipate...if the missing element is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *See Rosco, Inc. v. Mirror Lite Co.*, 304 F.3d 1373, 1380 (Fed. Cir. 2002). Further, "[i]nherent anticipation requires that the missing descriptive material is necessarily present, not merely probably or possibly present, in the prior art." *Id.*

In this case, by disclosing the full-length Spp-24 protein, Keifer does not disclose a substantially purified BBP which increases the degree or rate of osteogenesis or calcification, for example, by BMP-2. This is because Keifer discloses the much larger Spp-24 protein, which when used in its entirety, inhibits osteogenesis by BMPs. *See* Declaration of Keyvan Behnam, at ¶ 9. Keifer does not disclose BBP except as part of the Spp-24 protein. Keifer does not in any way teach that a fragment of the Spp-24 protein disclosed increases the degree or rate of osteogenesis or calcification, including in combination with BMPs. Thus, one skilled in the art reading Keifer would not know that a particular fragment of the protein disclosed will increase the degree or rate of osteogenesis or calcification, for example, by BMPs. In fact, it was unexpected that a fragment derived from Spp-24, which completely inhibits bone formation, would increase the degree or rate of osteogenesis. Thus, Applicants respectfully submit that Keifer does not expressly or inherently disclose all of the elements of the claimed invention, and therefore, Keifer cannot anticipate the claimed invention.

The Examiner further claims that to read Keifer as not disclosing a fragment of Spp-24 that increases the degree or rate of osteogenesis or calcification by BMP-2 is to argue that Applicants have themselves not enabled BBP. However, Applicants have enabled BBP, the claimed fragment of Spp-24 that increases the degree or rate of osteogenesis or calcification by BMP. Despite the fact that the full-length protein Spp-24 contains the sequence for BBP,

Spp-24 and BBP are physically in size and conformation different, and as a result do not have the same function. *See* Declaration of Keyvan Behnam, at ¶¶ 9-11.

As Dr. Behnam explains in his Declaration, proteins that include different amino acid sequences may have different sizes and conformations and thus different functions. *See* ¶ 5. Dr. Behnam also provides an example of this principle by describing the results of a study in which different fragments of the Spp-24 protein had differing effects on bone formation. *See* Declaration of Keyvan Behnam, at ¶ 9. Of the four protein fragments tested, two were shown to inhibit bone formation, while the other two slightly increased bone formation when given in small doses. *See id.* Further, each of the four fragments tested included the BBP sequence. *See id.* Thus, it is not the case that an amino acid sequence that includes the sequence for BBP will necessarily increase the degree or rate of osteogenesis or calcification. In fact, the opposite has been shown. Therefore, Applicants respectfully submit that claims 1, 3-4, 12, 13, 25, and 40 are not expressly or inherently anticipated by Keifer.

Claims 1, 3, 4, 12, 13, 22, 25, and 38-40 also stand rejected under 35 U.S.C. §102(b) as being anticipated by Price (WO 96/21006). However, the Price reference has similar deficiencies as the Keifer reference. The Examiner contends that Price teaches a peptide comprising an amino acid sequence that includes the claimed SEQ ID NO: 1. The Examiner also contends that by disclosing an amino acid sequence that includes the sequence for BBP, Price also inherently anticipates the claimed effect of the BBP peptide. Applicants respectfully disagree with the Examiner's interpretation of Price's teaching. Applicants respectfully contend that Price, like Keifer, teaches the use of the entire Spp-24 protein, not the BBP peptide. As discussed above, the full Spp-24 protein will act to completely inhibit BMP activity. *See* Declaration of Keyvan Behnam, at ¶ 9. In contrast, the claimed peptide will increase the degree or rate of osteogenesis, for example, in combination with BMPs. Price does not expressly or inherently disclose the use of the specific 19 amino acid fragment comprising BBP that will function as claimed. As such, Price does not expressly or inherently anticipate the claimed peptide.

CONCLUSION

In view of the foregoing, Applicants respectfully submit that Claims 1, 3-5, 11-13, 22, 23, 25, and 38-43 are in allowable form, and the application is now in condition for allowance. Applicants request the Examiner to indicate all claims as allowable, and the pass the application to issue.

The Commissioner is authorized to charge any additional fees or credit any overpayments associated with this Amendment to Deposit Account 13-0206. Applicants further invite the Examiner to contact the undersigned representative at the telephone number below to discuss any matters pertaining to the present Application. The Examiner is requested to contact the undersigned if the Examiner has any questions concerning this Response, or if it will expedite the progress of this application.

Respectfully submitted,

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Date: July 18, 2011

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Enclosures:

Declaration of Keyvan Behnam